ORIGINAL ARTICLE

Multisite Investigation of Traumatic Brain Injuries, Posttraumatic Stress Disorder, and Self-reported Health and Cognitive Impairments

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Context: Few large-scale, multisite investigations have assessed the development of posttraumatic stress disorder (PTSD) symptoms and health outcomes across the spectrum of patients with mild, moderate, and severe traumatic brain injury (TBI).

Objectives: To understand the risk of developing PTSD symptoms and to assess the impact of PTSD on the development of health and cognitive impairments across the full spectrum of TBI severity.

Design: Multisite US prospective cohort study.

Setting: Eighteen level I trauma centers and 51 non–trauma center hospitals.

Patients: A total of 3047 (weighted n=10 372) survivors of multiple traumatic injuries between the ages of 18 and 84 years.

Main Outcome Measures: Severity of TBI was categorized from chart-abstracted *International Classification of Diseases, Ninth Revision, Clinical Modification* codes. Symptoms consistent with a *DSM-IV* diagnosis of PTSD were assessed with the PTSD Checklist 12 months after injury. Self-reported outcome assessment included the 8 Medical Outcomes Study 36-Item Short Form Health Survey health status domains and a 4-item assessment of cognitive function at telephone interviews 3 and 12 months after injury.

Results: At the time of injury hospitalization, 20.5% of patients had severe TBI, 11.7% moderate TBI, 12.9% mild TBI, and 54.9% no TBI. Patients with severe (relative risk, 0.72; 95% confidence interval, 0.58-0.90) and moderate (0.63; 0.44-0.89) TBI, but not mild TBI (0.83; 0.61-1.13), demonstrated a significantly diminished risk of PTSD symptoms relative to patients without TBI. Across TBI categories, in adjusted analyses patients with PTSD demonstrated an increased risk of health status and cognitive impairments when compared with patients without PTSD.

Conclusions: More severe TBI was associated with a diminished risk of PTSD. Regardless of TBI severity, injured patients with PTSD demonstrated the greatest impairments in self-reported health and cognitive function. Treatment programs for patients with the full spectrum of TBI severity should integrate intervention approaches targeting PTSD.

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TRAUMATIC BRAIN INJURY (TBI) constitutes a major public health problem for both veteran and civilian trauma-exposed patient populations.[1-7] The US involvement in the current Iraq and Afghanistan conflicts has brought the interrelationship between TBI and posttraumatic stress disorder (PTSD) to the forefront of medical research, commentary, and practice.[8-19] Many earlier studies of TBI and PTSD focused on injured civilians presenting with a full spectrum of mild, moderate, and severe TBI.[20-33] More recent published investigations have focused on returning soldiers with mild TBI[1,34,35] and the substantial number of wounded combat veterans who incur varying degrees of TBI in conjunction with multiple injuries to other body regions.[36-40]

This growing body of literature documents that PTSD symptoms can develop after mild, moderate, and severe TBI.[1,20,21,23,30,31,34,41] Although it has frequently been suggested that the impaired memory of an event characteristic of increasingly severe brain injury could be associated with a diminished risk of PTSD,[19,21,26,27,42,43] literature review revealed few investigations that have directly compared the development of PTSD across TBI severity subgroups.[28] Most previous investigations have not included large enough samples of patients with mild, moderate, severe, and no TBI to allow for comparisons of PTSD rates across the full spectrum of TBI severity. In studies that

have included examination of other associated injuries, the composite injury severity score (ISS) has been used[36,44]; the ISS does not facilitate assessments of the occurrence of injuries to specific body regions, such as disfiguring facial injuries, that may be associated with both head injury and the development of PTSD.[38,45-47]

Investigations in veterans and civilians now document that PTSD and other comorbid psychiatric disorders make an independent contribution to a broad profile of health and cognitive impairments after mild TBI.[1,34,35] Bryant and colleagues[48] reported that, in a large sample of civilian injury survivors, functional impairment was related to the development of a spectrum of anxiety and depressive disorders rather than mild TBI.

An unanswered question is whether observations linking PTSD to adverse health outcomes extend to other patients experiencing more severe head injuries. Previous investigation in patients with multiple trauma suggests that longitudinal changes in cognition may be the outcome most clearly linked to baseline TBI severity after an injury hospitalization.[49] Investigation in noninjured veterans suggests that PTSD is independently associated with cognitive impairments as documented by neuropsychological assessment.[50] These combined observations raise questions regarding the nature and strength of the association between PTSD and cognitive impairments across the full spectrum of TBI severity.

The National Study on the Costs and Outcomes of Trauma (NSCOT) is the only multisite US investigation to date to observe PTSD symptom occurrence in a large cohort of patients who had sustained the full spectrum of mild, moderate, severe, and no TBI injuries.[51] The present analysis of the NSCOT data capitalizes on the large numbers of patients with mild, moderate, severe, and no TBI. The analysis also provides the ability to assess severity of injury to other body regions and to prospectively evaluate the impact of TBI severity on the occurrence of symptoms consistent with a screening diagnosis of PTSD 12 months after injury. As with most PTSD studies in injured cohorts to date,[33,40,52-62] previous NSCOT PTSD analyses used a composite ISS rather than breaking down injury severity into discrete body regions or head injury subtypes.[63,64] Further analyses of the large NSCOT sample afforded the opportunity to assess the associations between TBI severity, PTSD, and self-reported health and cognitive outcomes while adjusting for relevant demographic and clinical characteristics.

The investigators hypothesized that greater TBI severity would be associated with a diminished risk of symptoms consistent with a screening diagnosis of PTSD, even after adjustments for relevant demographic and clinical characteristics. The study also hypothesized that a screening diagnosis of PTSD would be associated with a broad spectrum of self-reported functional impairments across mild, moderate, severe, and no TBI severity subgroups. Finally, the investigation sought to perform an in-depth exploration of the interrelationships between TBI severity, PTSD, and acute neurologic deficits and long-term impairments in self-reported cognitive function.

METHODS

OVERVIEW OF THE NSCOT STUDY

The NSCOT was a multisite prospective cohort study designed to assess physical and mental health outcomes after hospitalization for traumatic injury.[51,63-65] All level I trauma centers and large non–trauma center hospitals were identified within US metropolitan statistical areas; states included were California, Florida, Illinois, Indiana, Maryland, Massachusetts, Michigan, New Jersey, New York, North Carolina, Pennsylvania, and Washington. Patients were enrolled from 69 hospitals. Eighteen of 27 (66.7%) level I trauma centers and 51 of 124 (41.1%) non–trauma center hospitals agreed to participate. The study was approved by the institutional review board of each of the participating hospitals. Informed consent was obtained from all participants before the conduct of patient assessments.

English- and Spanish-speaking patients aged 18 to 84 years were eligible for the study if they arrived alive at participating hospitals and were treated for moderate to severe injuries as defined by at least 1 injury with an Abbreviated Injury Scale (AIS) score of 3 or greater.[66] Patients were not eligible for enrollment if they were incarcerated at the time of injury, were 65 years or older, had treatment delays in excess of 24 hours, or had a first listed diagnosis of hip fracture or major burn.

Data regarding the episode of acute care was obtained by medical record review by trained nurse abstractors. Research nurses were trained in the chart abstraction procedure by the study investigators (F.P.R. and A.N.) and in the AIS coding procedure by the developers of the scale.[51,63-65]

Telephone assessments were conducted at 3 and 12 months after hospital discharge. Interviewers were experienced with telephone surveys and subsequently received additional specific training on the administration of the NSCOT assessment instruments (see also Mackenzie et al[51]). Telephone interview by proxy was allowed if the study participant was unable to be interviewed because of postinjury limitations, including severe brain injury.[51,67,68] At 3 months, 11.3% of interviews and, at 12 months, 10.0% of interviews were completed by proxies.

STUDY ASSESSMENT AND MEASURES

AIS and Maximum AIS

Severity of injury by body region was coded by means of the AIS to determine the Maximum AIS (MAXAIS) injury score.[66] The AIS was designed 30 years ago and is the most widely accepted anatomic measure of injury severity.[69] The MAXAIS has been shown to be highly correlated with threat to life as well as postinjury disability and quality of life.[70] Calculated as the highest AIS score for a single injury received, the MAXAIS performs well as a single measure of injury severity with an area under the receiver operating characteristic curve of 0.88 for mortality in a national database of more than 75 000 patients.[71]

Traumatic Brain Injury

The NSCOT used a quota sampling strategy to ensure that one-third of the patients had a head injury with an AIS score of 3 or higher and that the remainder had either a moderate-severe extremity injury or a moderate-severe injury to the chest or abdomen. Patients in these other 2 groups may have had a head injury, but it could not have an AIS score greater than 2. This strategy ensured that there was adequate representation of patients across the full spectrum of mild, moderate, severe, and no TBI severity subgroups.

In the NSCOT prospective cohort design, TBI was identified and categorized from hospital chart–abstracted *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*) codes indicative of traumatic injury. Specific *ICD-9-CM* codes used to prospectively identify TBIs included 800.0 to 801.9, 803.0 to 804.9, 850.0 to 854.1, and 959.01.[72,73] Severity of TBI was coded on the basis of a previously validated algorithm for hospitalized inpatients that assigned MAXAIS head injury scores of 1 to 2 to mild TBI severity, 3 to moderate TBI severity, and 4 or higher to severe TBI.[2,49]

Glasgow Coma Scale

The Glasgow Coma Scale (GCS) is a widely used scale for assessing level of consciousness after TBI.[74] The GCS score is based on the evaluation of 3 categories of neurologic function: eye opening, best verbal response, and best motor response. The GCS score ranges from 3 (most severely impaired) to 15 (no neurologic impairment). Lower GCS score has been shown to be highly correlated with greater duration of coma and increased posttraumatic amnesia.[75,76] In the NSCOT, GCS was assessed on initial admission to the hospital emergency department.

Self-reported Health and Functional Outcomes

The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) was administered during the 3- and 12-month postinjury telephone interviews.[77] In the present investigation, the 12-month SF-36 scores were used in the outcome assessment. The SF-36 has been used extensively to assess self-reported health and functional outcomes in injured patients.[49,64] The SF-36 contains 8 subscales that assess a broad profile of outcomes; subscales are scored from 0 to 100, with 100 equal to the best possible health state. Previous investigation using both internal consistency and test-retest methods have established reliability estimates for the 8 subscales of greater than 0.80.[77] Cronbach α for the 8 SF-36 subscales was 0.90 or greater at the 12-month assessments. Previous reports suggest that a single chronic medical condition, such as hypertension, diabetes, or depression, is associated with a 10-point or greater reduction in SF-36 subscale scores.[77]

Self-reported Cognitive Symptoms

A 4-item self-reported cognitive symptom scale was used to assess cognitive function at 3 and 12 months after the injury.[49] The items assessed 4 specific aspects of self-reported cognitive functioning, including reasoning and problem solving, memory, attention, and concentration and thinking. In a previous investigation, the scale demonstrated excellent internal consistency and construct validity.[49] In the present investigation, Cronbach α for the 4 items was 0.87 at the 3-month assessment and 0.90 at the 12-month assessment. The scale is scored from 0 to 100, with 100 equal to the best possible self-reported cognitive functioning.[49]

PTSD Symptoms

Symptoms of PTSD were assessed at the 12-month postinjury telephone interview with the civilian version of the PTSD Checklist (PCL).[78] The PCL is a 17-item self-report Likert response (1-5) questionnaire that assesses the intrusive, avoidant, and arousal PTSD symptom clusters. The measure has established reliability and validity across trauma-exposed populations.[79-82] In a study of motor vehicle crash survivors, Blanchard et al[83] reported that a PCL cutoff of 45 or greater has excellent sensitivity and specificity when compared with the criterion standard Clinician-Administered PTSD Scale. The PCL can be used to create an algorithm consistent with a diagnosis of PTSD by rating 1 intrusive, 3 avoidant, and 2 arousal symptoms with a score of 3 or greater as symptoms consistent with the *DSM-IV* diagnostic criteria. This algorithm was used to derive symptoms consistent with a diagnosis of PTSD at the 12-month postinjury time point.

STATISTICAL ANALYSIS

As in previously published NSCOT reports, we used sampling weights for all statistical analyses.[65] It was necessary to weight data on eligible participants because not all patients selected for inclusion in the study were enrolled in the NSCOT investigation. The sampling weights used in the NSCOT investigation consisted of the reciprocal product of 2 probabilities: the probability of being selected and the probability of being enrolled and having data abstracted from the medical record, given selection into the study. The reference population to which weighted inferences were made consisted of 15 440 patients who met or were projected to meet the inclusion criteria.

Multiple imputation techniques were used to account for missing covariates. Data were missing for less than 5% of patients for most NSCOT variables. Ten imputed data sets were created. To account for clustering within hospitals, robust standard errors were computed for each data set. All analyses were first performed on each imputed data set, and results from these 10 analyses were combined according to Rubin's rule to yield the final results.[84]

In the analyses, we first compared the demographic and clinical characteristics of patients who did and did not complete the 12-month telephone interview. The χ^2 and 2-tailed t test statistics were used for categorical and continuous variables, respectively, to assess for significant differences.

We next assessed the frequencies of patients incurring mild, moderate, and severe *ICD-9-CM*–documented head injury, as well as the frequency of patients incurring injuries with a MAXAIS score of 3 or higher to other body regions (ie, face, neck, thorax, abdomen, upper extremity, lower extremity, spine, and integument). Because we were interested in estimating the relative risks (RRs) and 95% confidence intervals (CIs) for developing PTSD, we used unadjusted Poisson regression with robust error variance to ascertain these univariate associations.[85,86] To obtain adjusted RRs and 95% CIs, we entered into a single Poisson regression model a dummy-coded variable for mild, moderate, and severe TBI (with the no-TBI group used as the reference), as well as variables for each body region with a MAXAIS score of 3 or higher (yes/no) that were significant at the $P < .05$ level in univariate analyses. Demographic and clinical characteristics previously shown to be associated with PTSD in hospitalized injured patients were also entered into the Poisson regression model as covariates.[63,64] Covariates included were GCS score; age; sex; ISS; race/ethnicity; injury type (intentional vs unintentional); marital status; insurance status; education; preinjury cigarette smoking; benzodiazepine use before the injury admission; hospital record documenting history of depressive, anxiety, alcohol, drug, or other mental health diagnosis; intensive care unit admission (yes/no); mechanical ventilation (yes/no); intubation (yes/no); emergency department heart rate; medical comorbidities; and SF-36 bodily pain, and mental health symptom subscales at the 3-month postinjury time point. Symptoms consistent with a screening diagnosis of PTSD on the PCL at the 12-month postinjury assessment were the dependent variable.

We next assessed 12-month SF-36 scale scores for patients with and without PTSD, stratified by mild, moderate, severe,

Table 1. Associations Between Traumatic Brain Injury Subtype and Location of Severe Bodily Injuries[a]

Injury Type	Total N=3047 (10372)[b] No.	Total N=3047 (10372)[b] Weighted No.	Traumatic Brain Injury, %[b] None n=1659(5691)	Mild n=413(1342)	Moderate n=367(1216)	Severe n=608 (2123)[a]	$F_{3,66}$	*P* Value
Severe facial								
No	2949	9958	97.9	95.9	91.0	93.8	3.8	.01
Yes	98	414	2.1	4.1	9.0	6.2		
Severe integument								
No	3031	10316	99.4	99.1	99.3	99.9	2.2	.10
Yes	16	56	0.6	0.9	0.7	0.1		
Severe lower extremity								
No	2122	7036	56.2	69.2	89.3	86.0	13.4	<.001
Yes	925	3336	43.8	30.8	10.7	14.0		
Severe upper extremity								
No	2711	9120	86.0	82.8	92.1	93.9	7.2	<.001
Yes	336	1252	14.0	17.2	7.9	6.1		
Severe thorax								
No	2036	6871	66.1	48.6	73.1	73.8	4.8	.004
Yes	1011	3501	33.9	51.4	26.9	26.2		
Severe spinal								
No	2825	9477	92.4	86.8	93.5	90.3	2.0	.12
Yes	222	895	7.6	13.2	6.5	9.7		
Severe abdomen								
No	2705	9283	86.6	86.9	94.5	96.1	5.4	.002
Yes	342	1089	13.4	13.1	5.5	3.9		
Severe neck								
No	3028	10286	99.6	98.3	100.0	98.0	327.8	<.001
Yes	19	86	0.4	1.7	0	2.0		

[a] Severe injury indicates a Maximum Abbreviated Injury Scale score of 3 or greater.[70]
[b] Weighted numbers are given in parentheses.

and no TBI groups. We first conducted univariate analyses and used 2-tailed *t* tests to compare SF-36 scale scores for patients with and without PTSD. These were followed by linear regression analyses that assessed for the association between PTSD and SF-36 scale scores across TBI subgroups while adjusting for demographic and clinical characteristics.[63,64]

Next, 3- and 12-month cognitive scale scores were compared for patients across the 4 TBI subgroups. An adjusted, mixed-model regression was used to assess the association between TBI severity and self-reported cognitive impairments over time.[63,64] We next assessed differences in 12-month postinjury cognitive scale scores for patients with and without PTSD stratified by TBI status (ie, none, mild, moderate, or severe). Four linear regressions were used to assess for an association between PTSD and self-reported cognitive impairment while adjusting for covariates (as listed earlier[63]).

Finally, we performed sensitivity analyses for the multivariate regressions by means of both a continuous PCL score and an alternative PCL dichotomous cutoff of 45 or greater[83] instead of PTSD diagnostic screening criteria. To assess the impact of proxy interviews, all analyses were conducted with and without proxy interview data. Analyses were conducted with the SAS 9.2 (SAS Institute Inc, Cary, North Carolina) and STATA 10 (StataCorp, College Station, Texas) data analytic software.

RESULTS

A total of 5043 (weighted N=14 477) patients were eligible for the study. Of these, 1245 patients (weighted n=1381) either died in the hospital or died in the days and weeks after hospitalization. A total of 3798 patients (weighted n=13 096) were included in the 3-month assessment; 90 died after the 3-month interview (weighted n=204), and 661 were lost to follow-up (weighted n=2520). A total of 3047 patients (weighted n=10 372), or 82.2% of 3708 eligible injury survivors, completed the 12-month follow-up interview. Patients lost to follow-up were significantly more likely to be younger (mean age, 38.4 years for those lost to follow-up vs 43.0 years for those who completed the interview; $t_1=3.7$, $P<.001$) and intentionally injured (32.2% vs 16.4%; $\chi^2_1=12.7$, $P=.001$). Relative to white patients, African American (26.2% vs 15.3%; $\chi^2_1=11.4$, $P=.001$) and Latino (28.7% vs 15.3%; $\chi^2_1=6.0$, $P=.02$) patients were more likely to be lost to follow-up. There were no significant differences in rates of loss to 12-month follow-up for patients in the severe (17.2%), moderate (13.3%), mild (17.5%), and no (22.0%) TBI subgroups ($\chi^2_3=5.7$, $P=.14$).

At the time of injury hospitalization, 20.5% of patients (2123 of 10 372) had experienced severe TBI, 11.7% (1216) moderate TBI, 12.9% (1342) mild TBI, and 54.9% (5691) no TBI. Patients with severe and moderate TBI were more likely to also incur severe facial injuries (**Table 1**). In contrast, patients with mild and no TBI were more likely to incur extremity, thoracic, and abdominal injuries (Table 1). Patients in the no-TBI group had significantly lower injury severity (mean [SD] ISS, 13.5[14.4]) relative to patients with severe (26.6 [19.2]), moderate (17.2 [14.4]), and mild (17.9 [15.9]) TBIs ($F_{3,68}=188.2$, $P<.001$).

At the 12-month postinjury time point, 21.8% of patients (2228 of 10 203) endorsed symptoms consistent

Table 2. Associations Between TBI Subtype, Other Bodily Injury, and PTSD Symptoms 12 Months After Hospital Admission[a,b]

Injury Type	Total N=2993 (10 203)[c] No.	Total N=2993 (10 203)[c] Weighted, No. (%)	% PTSD n=602 (2228)[b,c]	% No PTSD n= 2391 (7975)[b,c]	RR (95% CI) Unadjusted	RR (95% CI) Adjusted[d]
TBI subtype						
None	1637	5618 (55.1)	24.1	75.9	1.00 [Reference]	1.00 [Reference]
Mild	406	1321 (12.9)	22.7	77.3	0.94 (0.69-1.27)	0.83 (0.61-1.13)
Moderate	358	1194 (11.7)	18.8	81.2	0.78 (0.58-1.05)	0.63 (0.44-0.89)
Severe	592	2070 (20.3)	16.8	83.2	0.70 (0.56-0.87)	0.72 (0.58-0.90)
Severe facial						
No	2895	9789 (95.9)	21.4	78.6	1.00 [Reference]	1.00 [Reference]
Yes	98	414 (4.1)	31.0	69.0	1.44 (1.16-1.79)	1.38 (1.02-1.86)
Severe neck						
No	2975	10 119 (99.2)	21.6	78.4	1.00 [Reference]	1.00 [Reference]
Yes	18	84 (0.8)	48.1	51.9	2.23 (1.17-4.22)	1.21 (0.86-1.69)
Severe abdomen						
No	2652	9116 (89.3)	21.3	78.7	1.00 [Reference]	1.00 [Reference]
Yes	341	1087 (10.7)	26.0	74.0	1.22 (1.05-1.42)	0.99 (0.81-1.21)
Severe spinal						
No	2774	9315 (91.3)	20.9	79.1	1.00 [Reference]	1.00 [Reference]
Yes	219	888 (8.7)	31.4	68.6	1.50 (1.25-1.80)	1.32 (1.17-1.49)
Severe thorax						
No	1994	6738 (66.0)	22.4	77.6	1.00 [Reference]	
Yes	999	3465 (34.0)	20.8	79.2	0.93 (0.68-1.26)	
Severe upper extremity						
No	2663	8971 (87.9)	21.9	78.1	1.00 [Reference]	
Yes	330	1232 (12.1)	21.7	78.3	0.99 (0.81-1.21)	
Severe lower extremity						
No	2086	6926 (67.9)	21.8	78.2	1.00 [Reference]	
Yes	907	3277 (32.1)	21.9	78.1	1.00 (0.84-1.20)	
Severe integument						
No	2977	10 147 (99.5)	21.8	78.2	1.00 [Reference]	
Yes	16	56 (0.5)	36.3	63.7	1.67 (0.77-3.61)	

Abbreviations: CI, confidence interval; PTSD, posttraumatic stress disorder; RR, relative risk; TBI, traumatic brain injury.
[a] Severe injury indicates Maximum Abbreviated Injury Scale score of 3 or greater.[70]
[b] Symptoms consistent with a diagnosis of PTSD as assessed with the PTSD Checklist.[78]
[c] Weighted numbers are given in parentheses.
[d] Adjusted for initial Glasgow Coma Scale score,[74] age, sex, injury severity score, race/ethnicity, injury type (intentional vs unintentional), marital status, insurance status, education, preinjury cigarette smoking, benzodiazepine use before the injury admission, hospital record documenting history of intubation (yes/no), heart rate in emergency department, medical comorbidities, Medical Outcomes Study 36-Item Short Form Health Survey[77] bodily pain, and mental health symptom subscales 3 months after injury. Empty cells in the adjusted regression represent associations that were not significant in the unadjusted analyses.

with a diagnosis of PTSD on the PCL. In univariate analyses, increasing severity of TBI was associated with a diminished risk of PTSD symptoms (**Table 2**). In the adjusted Poisson regression analysis, severe and moderate TBI remained associated with a diminished risk of PTSD symptoms relative to the no-TBI comparison group (Table 2). Severe facial and spinal cord injuries were also associated with an increased risk of PTSD symptoms (Table 2). In this adjusted analysis, ISS was not associated with the development of PTSD (RR, 1.00; 95% CI, 0.99-1.01).

The mean (SD) initial admission GCS score was 10.3 (9.6) for patients with severe TBI, 12.7 (7.3) for patients with moderate TBI, 13.6 (5.9) for patients with mild TBI, and 14.3 (4.6) for patients with no TBI. In analyses that adjusted for demographic and clinical characteristics, these comparisons achieved statistical significance ($F_{3,68}=57.0$, $P<.001$). In univariate (RR, 0.99; 95% CI, 0.95-1.01) and multivariate (0.99; 0.97-1.01) analyses, lower GCS score was not associated with a diminished risk of PTSD.

Across TBI subgroups, in univariate analyses patients with symptoms consistent with a diagnosis of PTSD demonstrated clinically and statistically significant reductions in SF-36 subscale scores relative to patients with no PTSD (**Table 3**). Most of these associations remained significant in regression models that adjusted for relevant demographic and clinical characteristics (Table 3).

Patients with the most severe head injuries demonstrated the lowest cognitive scale scores as well as more gradual cognitive improvements during the year after injury (**Figure 1**). Repeated-measures mixed-model regression analyses with 3- and 12-month cognitive scale scores as the dependent variable demonstrated a significant main effect for severe ($\beta=-8.34$, SE=1.11, $P<.001$), moderate ($\beta=-5.69$, SE=1.15, $P<.001$), and mild ($\beta=-2.06$, SE=1.09, $P=.06$) head injuries relative to the no-TBI comparison group.

At the 12-month postinjury time point, regardless of TBI severity, patients with PTSD consistently demonstrated significantly lower cognitive scale scores (all $P<.001$) relative to patients without PTSD (**Figure 2**). Ad-

Table 3. PTSD and Health and Cognitive Function Across Categories of TBI Severity Among 2993 Injured Patients[a]

		Outcome, Mean (SD)							
	n (Weighted n)	Physical Health	Role Impairment Due to Physical Function	Bodily Pain	General Health	Vitality	Social Function	Role Impairment Due to Emotional Function	Mental Health
Total									
No PTSD	2391 (7975)	43.5 (23.4)	41.1 (23.0)	46.3 (20.1)	48.2 (20.2)	48.3 (19.1)	48.1 (20.8)	48.1 (19.8)	51.6 (18.9)
PTSD	602 (2228)	31.7 (25.3)	30.3 (14.6)	34.7 (18.9)	34.7 (22.1)	35.8 (17.0)	31.6 (22.3)	32.1 (18.0)	33.5 (22.4)
β[b]		7.1[c]	5.4[c]	6.1[c]	7.2[c]	7.2[c]	10.5[c]	10.7[c]	11.1[c]
No TBI									
No PTSD	1291 (4263)	42.7 (23.9)	40.8 (23.2)	45.8 (19.9)	48.6 (20.3)	48.8 (19.0)	48.5 (21.0)	48.3 (19.8)	52.3 (18.4)
PTSD	346 (1355)	30.8 (25.2)	30.1 (13.7)	34.5 (18.5)	34.8 (22.3)	36.1 (17.0)	32.0 (21.9)	32.5 (18.7)	33.7 (21.2)
β[b]		7.3[c]	5.1[c]	6.7[c]	8.4[c]	7.8[c]	10.4[c]	10.3[c]	12.0[c]
Mild TBI									
No PTSD	319 (1021)	42.2 (22.9)	39.7 (21.9)	43.8 (20.2)	46.8 (19.2)	47.4 (18.6)	47.3 (20.6)	47.7 (19.6)	50.1 (17.9)
PTSD	87 (300)	28.0 (22.5)	29.3 (14.0)	32.9 (17.6)	34.5 (20.9)	35.2 (15.1)	32.3 (23.3)	31.8 (17.1)	35.4 (22.7)
β[b]		6.1[d]	3.6[d]	3.2	4.4[d]	6.6[c]	9.2[c]	10.1[c]	8.5[c]
Moderate TBI									
No PTSD	291 (969)	46.8 (20.8)	43.8 (22.1)	47.7 (19.5)	48.7 (20.2)	47.8 (18.8)	48.4 (17.9)	49.2 (18.2)	50.4 (20.3)
PTSD	67 (225)	37.0 (25.3)	32.1 (17.2)	34.5 (17.9)	35.2 (20.8)	36.6 (15.4)	32.1 (20.9)	31.1 (16.1)	33.1 (20.8)
β[b]		6.1[e]	5.4[e]	8.1[c]	5.3[d]	3.5[e]	11.1[c]	12.2[c]	8.1[c]
Severe TBI									
No PTSD	490 (1722)	44.5 (23.1)	41.4 (23.1)	47.9 (20.3)	47.5 (20.6)	47.9 (19.9)	47.4 (21.6)	47.4 (21.0)	51.3 (19.8)
PTSD	102 (348)	34.9 (25.2)	30.7 (15.7)	37.1 (21.2)	34.1 (23.4)	34.8 (19.2)	29.4 (23.4)	31.2 (17.1)	31.4 (26.4)
β[b]		4.8[d]	5.7[c]	3.7[d]	5.5[d]	7.6[c]	11.1[c]	9.8[c]	12.5[c]

Abbreviations: PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.

[a] The PTSD Checklist[78] was used to determine symptoms consistent with a diagnosis of PTSD, and health status was assessed with the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36).[77] Unadjusted means for SF-36 scale scores are presented.

[b] Linear regression β coefficients for PTSD are presented where regressions are adjusted for initial Glasgow Coma Scale score[74]; age; sex; injury severity score; race/ethnicity; injury type (intentional vs unintentional); marital status; insurance status; education; preinjury cigarette smoking; preinjury benzodiazepine use; hospital record documenting history of depressive, anxiety, alcohol, drug, and/or other mental health diagnosis; intensive care unit admission (yes/no); mechanical ventilation (yes/no); intubation (yes/no); heart rate in emergency department; medical comorbidities; and SF-36 bodily pain and mental health symptom subscales 3 months after injury.

[c] $P<.001$.

[d] $P<.01$.

[e] $P<.05$.

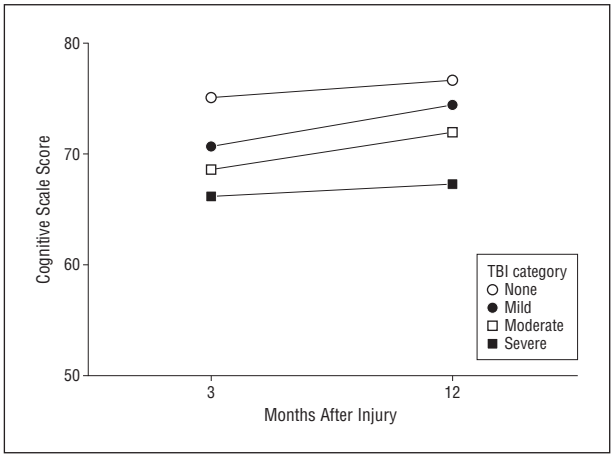

Figure 1. Cognitive scale score by traumatic brain injury (TBI) category at 3 and 12 months after injury.

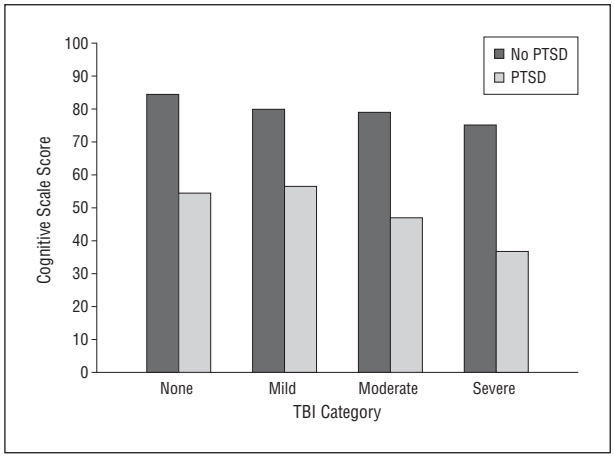

Figure 2. Twelve-month posttraumatic stress disorder (PTSD) and cognitive scale scores across categories of traumatic brain injury (TBI).

justed regression analysis identified a significant association between PTSD and lower cognitive scale scores in the severe TBI (β=24.20, SE=5.50, $P<.001$), moderate TBI (β=16.25, SE=5.68, $P=.01$), mild TBI (β=15.34, SE=4.70, $P=.002$), and no TBI (β=22.09, SE=1.52, $P<.001$) subgroups.

Sensitivity analyses that used a continuous PCL score and an alternative PCL dichotomous cutoff of 45 or greater[83] instead of PTSD diagnostic screening criteria did not substantially alter the magnitude, pattern, or significance of the associations between TBI subgroup, PTSD, and functional outcomes (ie, the results presented in

Table 2, Table 3, and Figure 2). Also, analyses that excluded all interview data obtained by proxy did not substantially alter the magnitude, pattern, or significance of the observed associations between TBI subgroup, PTSD, and functional outcomes.

COMMENT

Recent commentary and investigation have focused extensively on the associations between TBI, PTSD, and health status among returning veterans of the current Central Asian conflicts.* A key criterion for the progression of epidemiologic knowledge is consistency of observations across exposed populations.[87] The prospective design and large civilian sample of patients with head and other bodily injuries afforded by the present NSCOT analyses allow for a unique contribution to this evolving literature on TBI and PTSD.

The present investigation demonstrates in a large prospectively observed cohort that patients with more severe TBI have a diminished risk of developing symptoms consistent with a diagnosis of PTSD. Although lower GCS score was significantly associated with TBI severity, the investigation did not find a direct association between immediate postinjury neurologic deficits as measured by the GCS and the later development of diminished PTSD symptoms. Although duration of coma and posttraumatic amnesia were not directly measured in the NSCOT, previous investigations have established that lower GCS score is associated with lengthier coma and amnesia.[75,76] The diminished risk of PTSD by TBI severity is consistent with the possibility that the mechanism involves impaired consolidation of traumatic memories[19,20,27,43]; however, the immediate level of consciousness at the time of injury does not appear to be the most important factor in this process. Future investigations could explore alternative etiologic mechanisms including temporal variations in the generation of posttraumatic affective responses, implicit coding of sensory perceptual experiences, and neurobiological factors that may influence physiologic, behavioral, and emotional responses after TBI.[13,19,20,27,43]

To our knowledge, this is the first investigation to document that severe facial and spinal cord injuries are independently associated with an increased risk of symptoms consistent with a diagnosis of PTSD. In these analyses, which included detailed assessments of injury to specific body regions, the composite ISS was not associated with the development of PTSD symptoms.[19,36] Co-occurring head and facial injuries have been commonly described among wounded Central Asian veteran survivors of blast injuries/multiple trauma.[37,38] A previous smaller-scale investigation suggests that disfiguring injuries may amplify posttraumatic symptoms by increasing concerns about body image and social acceptance,[45] and other studies have described PTSD symptoms in the aftermath of spinal cord injury.[88,89]

The investigation corroborates and extends previous studies by demonstrating a strong independent association between PTSD and a broad profile of self-reported health and cognitive functioning impairments in patients with the full spectrum of mild, moderate, and severe TBI.[52,61,90-95] Other recent investigations have focused on PTSD-related health and cognitive limitations among returning veterans with and without mild TBI.[1,34,35,50]

There are a number of important limitations to this investigation. One such limitation is the restriction of psychiatric outcomes to PTSD; recent investigation by Bryant et al[48] suggests that multiple psychiatric diagnoses, including but extending beyond PTSD, may be associated with TBI. Thus, limitations in health-related and cognitive-related functioning observed in the present investigation could be partly explained by other mental health symptoms. The analyses conducted at the 12-month time point assessing the associations between PTSD symptoms, health outcomes, and self-reported cognitive impairments are cross-sectional. The investigation cannot rule out the possibility that self-reported health and cognitive impairments could be contributing to the worsening of PTSD symptoms. Of note, previous prospective longitudinal investigations in injured youth and adults suggest that early high levels of PTSD symptoms may influence the later development of poorer health outcomes.[61,92,93,95] Another limitation is that new cases of PTSD could not be determined because the design of the investigation did not allow for the assessment of preexisting PTSD.[48] The present investigation used MAXAIS to classify TBI severity; although there are a number of methods for classifying TBI severity, the use of the MAXAIS classification framework allowed for head injury severity to be assessed prospectively and did not require retrospective recall of the physical injury trauma. An additional limitation is the exclusive reliance on self-reported health and cognitive functional outcomes; it cannot be ruled out, for example, that what is being described as self-reported cognitive function throughout this article is really patient cognitive complaints. The investigation is further limited by the use of proxy interviews in a subsample of injured trauma survivors. Finally, the present investigation did not include in-depth assessments of duration of coma, posttraumatic amnesia, memory of the traumatic event, neuropsychological evaluation of cognitive impairments, or neuroradiologic findings.[19,27,43,96,97]

CONCLUSIONS

Traumatic brain injury represents a dynamic spectrum of physiologic and cognitive dysfunction that exerts effects at the level of the individual neuron, neural networks, and ultimately more global cognition and health.[7] The present investigation adds to a growing body of research that suggests that psychological factors play a substantial role in TBI-related impairments in self-reported health and cognition function. A key assumption in the TBI literature has been that health and cognitive impairments in more severely injured patients with TBI would be less affected by the presence of PTSD. For example, it has been suggested that, in moderate and severe TBI, the

References 1, 8, 10-12, 14, 15, 17, 19, 34-40.

meticulous assessment of neurocognitive deficits underlying functional impairments may be an essential and valuable component of ongoing clinical care; in contrast, for mild TBI, the assessment of neurocognitive deficits has been suggested to be less conclusive, presumably because of the predominating influence of PTSD and other psychological factors.[11] The misattribution of health- and cognitive-related functional impairments to brain injury alone has the potentially detrimental implication that recovery from TBI depends predominantly on neurologic factors.[10] The results of the present investigation suggest that treatment programs for the full spectrum of injured patients with mild, moderate, and severe TBI could productively integrate multifaceted interventions targeting PTSD.[98-102]

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